Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1644PNH

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Apr 08	"Ask CAS" for self-help around the clock
NEWS	3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	4	Apr 09	ZDB will be removed from STN
NEWS	5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS	9	Jun 03	New e-mail delivery for search results now available
NEWS	10	Jun 10	MEDLINE Reload
NEWS	11	Jun 10	PCTFULL has been reloaded
NEWS	12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS	13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS	14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS	15	Jul 30	NETFIRST to be removed from STN
NEWS	16	Aug 08	CANCERLIT reload
NEWS	17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	18	Aug 08	NTIS has been reloaded and enhanced
NEWS	19	Aug 09	JAPIO to be reloaded August 18, 2002

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:51:15 ON 12 AUG 2002

=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 08:51:31 ON 12 AUG 2002

FILE 'EMBASE' ENTERED AT 08:51:31 ON 12 AUG 2002

FILE 'BIOSIS' ENTERED AT 08:51:31 ON 12 AUG 2002

FILE 'SCISEARCH' ENTERED AT 08:51:31 ON 12 AUG 2002

FILE 'CAPLUS' ENTERED AT 08:51:31 ON 12 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


```
=> s allergen
L1      101695 ALLERGEN

=> s l1 and modified
L2        2366 L1 AND MODIFIED

=> s l2 and crosslink
L3           1 L2 AND CROSSLINK

=> d l3 cbib abs

L3   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
2001:676622   Document No. 135:225857  Microbial delivery system.  Caplan,
     Michael (Panacea Pharmaceuticals, LLC, USA).  PCT Int. Appl. WO 2001066136
     A2 20010913, 57 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ,
     BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES,
     FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
     LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL,
     PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
     YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF,
     CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML,
     MR, NE, NL, PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.
     APPLICATION: WO 2000-US33121 20001206.  PRIORITY: US 2000-PV195035
     20000306.
AB   The present invention provides methods and compns. for treating or
     preventing allergic responses, particularly anaphylactic allergic
     responses, in subjects who are allergic to allergens or
     susceptible to allergies.  Methods of the present invention utilize
     administration of microorganisms to subjects, where the microorganisms
     produce allergens and protect the subjects from exposure to the
     allergens until phagocytosed by antigen-presenting cells.
     Particularly preferred microorganisms are gram-neg. bacteria, gram-pos.
     bacteria, and yeast.  Particularly preferred allergens are
     proteins found in foods, venoms, drugs and latex that elicit allergic
     reactions and anaphylactic allergic reactions in individuals who are
     allergic to the proteins or are susceptible to allergies to the proteins.
     The proteins may also be modified to reduce the ability of the
     proteins to bind and crosslink IgE antibodies and thereby reduce
     the risk of eliciting anaphylaxis without affecting T-cell mediated
     Th1-type immunity.


=> d his
```

(FILE 'HOME' ENTERED AT 08:51:15 ON 12 AUG 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:51:31 ON 12 AUG 2002

L1 101695 S ALLERGEN
L2 2366 S L1 AND MODIFIED
L3 1 S L2 AND CROSSLINK

=> s l2 and tyrosine coated
L4 0 L2 AND TYROSINE COATED

=> s l1 and tyrosine
L5 407 L1 AND TYROSINE

=> s l5 and crosslinked
L6 1 L5 AND CROSSLINKED

=> d l6 cbib abs

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
1985:202216 Document No. 102:202216 500-MHz Proton NMR studies of ragweed **allergen** Ra5. Vidusek, David A.; Roberts, Mary F.; Goodfriend, Lawrence (Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA). Biochemistry, 24(11), 2747-53 (English) 1985. CODEN: BICHAW. ISSN: 0006-2960.

AB The soln. conformation of short ragweed **allergen** Ra5, a protein of 45 amino acid-residues **crosslinked** with 4 disulfide bridges, was investigated by 1H-NMR spectroscopy at 500 MHz. The arom. region, which contains resonances from 3 **tyrosines** and 2 tryptophans, has been partially assigned. Two **tyrosines** titrate with a pK of 10.2; a third **tyrosine** is buried under the tryptophan resonances, and its pK could not be detd. The 2 tryptophans reside in different microenvironments; the resonances of one are very similar to those found in random coil structures while the other has dramatically shifted peaks. Nuclear Overhauser effect (NOE) difference spectroscopy is used to define 2 distinct spin-diffusion systems for the arom. residues and to further identify several methyl-contg. amino acids involved in these systems. Assignments in the Me region are based on selective decoupling, chem. shifts, NOE difference spectra, and 2-D J-resolved and 2-D J-correlated spectroscopy (COSY) methodol. A unique ring-current shifted Me doublet in the Ra5 spectrum titrates into the bulk Me region with a pK of 10.2. Examn. of the COSY map suggests that this resonance belongs to either leucine-1 or isoleucine-38. Chem. removal of the N-terminal leucine did not affect the ring-current-shifted Me. Therefore, this unique resonance has been assigned to the Me of isoleucine-38. With this assignment and the spin-diffusion behavior of the arom. residues, it is possible to suggest disulfide assignments as well as specific structural features of Ra5 consistent with the toxin-agglutinin fold proposed by J. Drenth et al. (1980).

=> dup remove l5
PROCESSING COMPLETED FOR L5
L7 249 DUP REMOVE L5 (158 DUPLICATES REMOVED)

=> s l7 and adsorbed
L8 40 L7 AND ADSORBED

=> dup remove l8
PROCESSING COMPLETED FOR L8
L9 40 DUP REMOVE L8 (0 DUPLICATES REMOVED)

=> d l9 1 cbib abs

L9 ANSWER 1 OF 40 MEDLINE
2001694043 Document Number: 21605984. PubMed ID: 11738737. Safety evaluation of a glutaraldehyde modified **tyrosine** **adsorbed** housedust mite extract containing monophosphoryl lipid A (MPL) adjuvant: a new allergy vaccine for dust mite allergy. Baldrick P; Richardson D; Wheeler A W. (Covance Laboratories Ltd., Otley Road, Harrogate, North Yorkshire HG3 1PY, UK.) VACCINE, (2001 Dec 12) 20 (5-6) 737-43. Journal code: 8406899. ISSN: 0264-410X. Pub. country: England: United Kingdom. Language: English.

AB A new allergy vaccine is currently under clinical evaluation for the prevention or relief of symptoms caused by specific housedust mites. It consists of a 50:50 mixture of the mite Dermatophagoides pteronyssinus and D. farinae protein derived from aqueous extracts of the mites which is chemically modified by glutaraldehyde and **adsorbed** onto L-**tyrosine** with addition of the immunostimulatory adjuvant, monophosphoryl lipid A (MPL) "Polymite". A specific preclinical safety testing strategy was developed to support clinical use and comprised single and repeat dose toxicity, reproduction toxicity and local tolerance studies. Dose levels of up to 0.5ml for the mouse and up to 1ml for both the rat and the rabbit were used. Overall, the product was shown to produce no toxicological findings of significance at levels greatly in excess to those proposed for clinical use. A not unexpected, but relatively minor, immunostimulatory effect was seen following repeated dosing (once weekly for 13 weeks) at 1ml per rat; the Polymite formulation also resulted in injection site reaction which can largely be attributed to the presence of **tyrosine**. No reproduction toxicity was found.

=> d l8 1-40 cbib abs

L8 ANSWER 1 OF 40 MEDLINE
2002102119 Document Number: 21823094. PubMed ID: 11834183. Standardisation of glutaraldehyde-modified **tyrosine**-**adsorbed** tree pollen vaccines containing the Th1-inducing adjuvant, monophosphoryl lipid A (MPL). Hopkins M; Lees B G; Richardson D G; Woroniecki S R; Wheeler A W. (Allergy Therapeutics Ltd, West Sussex, UK.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (2001 Nov-Dec) 29 (6) 245-54. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB BACKGROUND: a new range of allergy vaccines has been developed by the introduction of a relatively new Th1-inducing adjuvant known as 3-deacylated monophosphoryl lipid A (MPL). MPL adjuvant is of natural origin, derived from the lipopolysaccharide of Salmonella minnesota R595. This adjuvant is incorporated in a glutaraldehyde-modified pollen extract **adsorbed** to L-**tyrosine** (Pollinex Quattro). A major potential benefit provided by MPL adjuvant is the promotion of a Th1 response which enhances the efficacy of allergy vaccination and can consequently allow a reduction in the number of injections required for treatment. The standardisation of Pollinex Quattro tree pollen allergy vaccine is described and we include details of some innovative analytical procedures. METHODS AND RESULTS: an essential feature of the analytical strategy is the assay of the MPL adjuvant using a recently developed HPLC technique. The adjuvant has a complex chemical structure and the analysis is illustrated in detail. We give a full picture of the vaccine standardisation by describing biochemical and immunological characterisation of the **allergen** extract, together with some brief manufacturing details. CONCLUSIONS: a high overall level of standardisation is illustrated by a number of different tests applied to all stages of vaccine manufacture. Tree pollen **allergen** potency is measured following the pollen extraction, chemical modification and formulation as a **tyrosine** adsorbate. Good batch-to-batch reproducibility is shown. The HPLC assay for MPL adjuvant showed high

quality resolution which did not vary when measuring raw material or when incorporated in the vaccine and the technically complex assay is shown to be reliable.

L8 ANSWER 2 OF 40 MEDLINE

2001694043 Document Number: 21605984. PubMed ID: 11738737. Safety evaluation of a glutaraldehyde modified **tyrosine adsorbed** housedust mite extract containing monophosphoryl lipid A (MPL) adjuvant: a new allergy vaccine for dust mite allergy. Baldrick P; Richardson D; Wheeler A W. (Covance Laboratories Ltd., Otley Road, Harrogate, North Yorkshire HG3 1PY, UK.) VACCINE, (2001 Dec 12) 20 (5-6) 737-43. Journal code: 8406899. ISSN: 0264-410X. Pub. country: England: United Kingdom. Language: English.

AB A new allergy vaccine is currently under clinical evaluation for the prevention or relief of symptoms caused by specific housedust mites. It consists of a 50:50 mixture of the mite Dermatophagoides pteronyssinus and D. farinae protein derived from aqueous extracts of the mites which is chemically modified by glutaraldehyde and **adsorbed** onto L-**tyrosine** with addition of the immunostimulatory adjuvant, monophosphoryl lipid A (MPL) "Polymite". A specific preclinical safety testing strategy was developed to support clinical use and comprised single and repeat dose toxicity, reproduction toxicity and local tolerance studies. Dose levels of up to 0.5ml for the mouse and up to 1ml for both the rat and the rabbit were used. Overall, the product was shown to produce no toxicological findings of significance at levels greatly in excess to those proposed for clinical use. A not unexpected, but relatively minor, immunostimulatory effect was seen following repeated dosing (once weekly for 13 weeks) at 1ml per rat; the Polymite formulation also resulted in injection site reaction which can largely be attributed to the presence of **tyrosine**. No reproduction toxicity was found.

L8 ANSWER 3 OF 40 MEDLINE

2001682811 Document Number: 21585804. PubMed ID: 11729351. A Th1-inducing adjuvant, MPL, enhances antibody profiles in experimental animals suggesting it has the potential to improve the efficacy of allergy vaccines. Wheeler A W; Marshall J S; Ulrich J T. (Allergy Therapeutics Ltd, Worthing, UK.. alan.wheeler@allergytherapeutics.com) . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Oct) 126 (2) 135-9. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Monophosphoryl lipid A (MPL) is a detoxified derivative of the lipopolysaccharide (LPS) moiety of Salmonella minnesota R595, which has retained immunostimulatory activities. MPL has been administered to many subjects in clinical trials as an adjuvant component of infectious disease vaccines and is currently a component of a licensed cancer vaccine, Melacine (Corixa Inc., Schering Plough). MPL has, in particular, been shown to promote Th1-type antigen specific responses. L-**tyrosine** is a depot adjuvant which is fully metabolisable and has been successfully employed in allergy vaccines for a number of years. METHODS: Mice were immunised with MPL adjuvant in conjunction with separate preparations of either ovalbumin or glutaraldehyde-modified ragweed pollen extract both coprecipitated with L-**tyrosine**. The specific antibody isotypes IgG1, IgG2a, IgG2b and also IgE were measured. Rats received booster injections of keyhole limpet haemocyanin (KLH) in conjunction with MPL adjuvant following priming with KLH in alum alone. KLH-specific antibody responses were measured. RESULTS: It was shown that a combination of L-**tyrosine** and MPL were synergistic in enhancing murine antigen specific IgG antibody responses without enhancing antigen specific IgE responses. Furthermore, this adjuvant combination promoted strong IgG2 antigen specific responses indicative of a Th1 directed response. In KLH sensitised rats, treatment with MPL was shown to prevent a secondary IgE antibody response when injected with booster injections of antigen. CONCLUSIONS: Immunisation of mice with two different antigens

adsorbed to L-**tyrosine** induced a Th1-skewed primary response when in conjunction with MPL adjuvant which also generally enhances a specific IgG response. Incorporation of MPL adjuvant in the immunisation of rats prevented a secondary specific IgE response. These results suggest that the employment of this new adjuvant in clinical allergy vaccination formulations may result in an improved efficacy which could be utilised in various ways to improve compliance.

L8 ANSWER 4 OF 40 MEDLINE

1999362317 Document Number: 99362317. PubMed ID: 10431101. Comparison of the efficacy and safety of two preseasonal regimens of glutaraldehyde modified, **tyrosine-adsorbed** parietaria pollen extract over a period of three years in monosensitive patients. Negro J M; Wheeler A W; Hernandez J; Youlten L J; Pascual A; Garcia-Selles F J; Pagan J A; Lopez-Sanchez J D; Miralles J C; Sarrio F; Milan J M; Contreras L G; Vidal D. (Allergology Section, H. U. "Virgen de la Arrixaca", El Palmar, Murcia, Espana.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1999 May-Jun) 27 (3) 153-64. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB The purpose of this study was to evaluate the clinical efficacy over a period of three years (1988-90) of two preseasonal dosage regimens of a Parietaria allergoid (Bencard **Tyrosine** Parietaria) in patients who were only sensitive to this pollen. Fifty patients were included (14 men and 36 women, age: mean, 28 years; range, 14-47 years). Twenty five patients (group A) were treated each january with the basic course of Bencard **Tyrosine** Parietaria. This consisted of injecting subcutaneously 0.5 ml from each of three vials, with one week between each injection. A further injection using the vial with the highest dose was given one week later. Each january and february, twenty five patients (group B) were treated with the basic course of Bencard **Tyrosine** Parietaria, repeating the last dose five times, with one week between each injection. Immunotherapy with a **tyrosine-adsorbed** Parietaria judaica allergoid is an effective method for mitigating nasal ($p < 0.0001$), bronchial ($p < 0.005$), conjunctival ($p < 0.001$) and palatal itching symptoms ($p < 0.0001$) in patients who are sensitive to this pollen. Sensitivity to Parietaria pollen, as verified by skin test and nasal challenge, decreased during immunotherapy ($p < 0.001$). Histamine release by peripheral blood basophils decreased during the course of the study, falling from 43.5 ng/ml to 12.3 ng/ml in group A and from 42.9 ng/ml to 10.0 ng/ml in group B; during the second and third years, IgG levels were increased one and four months after starting treatment with the extract, while this was not the case after ten months; IgE levels were also increased. Finally, overall tolerance to this immunotherapy product was good in almost all patients.

L8 ANSWER 5 OF 40 MEDLINE

94115598 Document Number: 94115598. PubMed ID: 1669569. Pollinex Parietaria (Bencard Parietaria), a new allergoid for treatment of patients sensitive to Parietaria pollen. Resta O; Carnimeo N; Foschino M P; Taylor I; Wheeler A W; Youlten L J. (Cattedra Fisiopatologia Respiratoria Ospedale Policlinico, Bari, Italy.) JOURNAL OF INVESTIGATIONAL ALLERGOLOGY AND CLINICAL IMMUNOLOGY, (1991 Apr) 1 (2) 129-37. Journal code: 9107858. ISSN: 1018-9068. Pub. country: Spain. Language: English.

AB Two matching groups each of eleven patients suffering from allergy to Parietaria pollen were treated either with **tyrosine-adsorbed** glutaraldehyde-modified extract of Parietaria judaica pollen (Bencard Parietaria/Pollinex Parietaria) or with alum-**adsorbed** pyridine-extract (Alavac). The side effects of therapy were similar in both groups and were mostly local in nature. Nasal symptoms were significantly less at the end of treatment in the group of patients treated with Pollinex. P. judaica-specific IgG levels were significantly higher in patients following treatment with Pollinex. The

majority of patients in both groups showed reduced nasal and/or skin sensitivity following therapy as measured by provocation testing. The results indicate that Pollinex Parietaria is an effective vaccine for the treatment of immediate hypersensitivity to Parietaria pollen.

L8 ANSWER 6 OF 40 MEDLINE
94115589 Document Number: 94115589. PubMed ID: 1669563. Hyposensitization therapy of Parietaria-sensitive patients with a **tyrosine adsorbed** allergoid, Pollinex Parietaria (Bencard Parietaria). Bonifazi F; Antonicelli L; Bilo M B; Pucci S; Taylor I H; Wheeler A W; Youlten L J. (Servizio Allergologia Respiratoria, Ospedale Generale Umberto I, Ancona, Italy.) JOURNAL OF INVESTIGATIONAL ALLERGOLOGY AND CLINICAL IMMUNOLOGY, (1991 Feb) 1 (1) 37-44. Journal code: 9107858. ISSN: 1018-9068. Pub. country: Spain. Language: English.
AB Thirty patients suffering from allergy to Parietaria pollen were treated with either a new **tyrosine-adsorbed** allergoid of Parietaria judaica pollen (Pollinex Parietaria) or a commercially available alum-**adsorbed** extract (Alavac) as control. A reduced response to nasal provocation was seen in 7 out of 11 patients following treatment with Pollinex and 1 out of 10 after control treatment. 9 out of 11 and 3 out of 10, respectively, showed reduced skin test activity. Patients who received Pollinex tended to have fewer nasal symptoms during the pollen season. Pollinex induced larger increases in P. judaica-specific IgG antibody than did the control product. Side effects of therapy were similar between the two groups of patients. Pollinex Parietaria thus shows good potential for the control of allergy to Parietaria pollen.

L8 ANSWER 7 OF 40 MEDLINE
90260471 Document Number: 90260471. PubMed ID: 2188335. [Hyposensitization in pollinosis. Results of a 3-year controlled study with 2 depot-allergoid grass pollen extracts: aluminum hydroxide-**adsorbed** allergoid and **tyrosine-adsorbed** allergoid]. Zur Hyposensibilisierung der Pollinose. Ergebnisse einer kontrollierten Studie uber drei Jahre mit zwei Depotallergoid-Graspollenextrakten: Aluminiumhydroxid-adsorbiertes Allergoid (AGD) und Tyrosin-adsorbiertes Allergoid (TA). Muhlethaler K; Wuthrich B; Peeters A G; Terki N; Girard J P; Frank E. (Dermatologische Klinik, Universitat Zurich.) SCHWEIZERISCHE RUNDSCHAU FUR MEDIZIN PRAXIS, (1990 Apr 3) 79 (14) 430-6. Journal code: 8403202. ISSN: 1013-2058. Pub. country: Switzerland. Language: German.
AB For controlled hyposensitization treatment over a period of three years 36 patients with confirmed grass pollen sensitization had been selected in 1986 and randomly distributed to receive preseasonal injection therapy: 23 patients were treated with an average of seven AGD (aluminium-**adsorbed** allergoid) injections, and 13 patients had received six TA (**tyrosine-adsorbed** allergoid) injections.
Evaluation of the trial data collected during three years of preseasonal treatment showed the following results of tolerance and efficacy: Systemic side-reactions registered during therapy were only mild and transient and occurred in the average after 3% of the AGD injections and after 10% of the TA injections. Local reactions over 5 cm diameter were registered after 7% in the AGD group and after 9% in the TA group. Before therapy there was no significant difference (p greater than 0.05) between the groups; after three years of therapy the AGD injections had resulted in a mean net rise of specific IgG of 220% (significant, p = 0.001); during the same time, TA injections had resulted in a final net increase of 10% (not significant, p greater than 0.05). Both treatment forms did not lead to any statistically relevant changes of specific IgE values. After three years of hyposensitization treatment, patients of both groups had improved; but an advantage was documented for patients treated with AGD on the basis of scores for objective assessment as well as for registered symptom and medication scores.

L8 ANSWER 8 OF 40 MEDLINE
85262442 Document Number: 85262442. PubMed ID: 3926854. Modified forms of **allergen** immunotherapy. Grammer L C; Shaughnessy M A; Patterson R. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1985 Aug) 76 (2 Pt 2) 397-401. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB There have been many attempts to modify **allergens** and thus to improve upon conventional immunotherapy, which has been proved effective but has several drawbacks. These include the risk of systemic reactions and the time and cost involved. The modifications have taken three major approaches. One approach, to impede **allergen** release from the site of deposition, has met with limited success. An example is alum precipitation, which has modestly reduced the number of injections and incidence of systemic reactions. A second approach, to suppress specific IgE production and to induce specific tolerance, has not been successful in man. The third approach, to reduce allergenicity while retaining immunogenicity of **allergens**, has been the most successful and appears to have the most promise. One example is polymerized **allergens**, which have been shown to be safe, efficacious, and immunogenic in multiple clinical trials. Other examples include allergoids and glutaraldehyde-treated, **tyrosine-adsorbed** **allergens**.

L8 ANSWER 9 OF 40 MEDLINE
85044593 Document Number: 85044593. PubMed ID: 6388401. Hyposensitization with a **tyrosine adsorbed** extract of Dermatophagoides pteronyssinus in adults with perennial rhinitis. A controlled clinical trial. Blainey A D; Phillips M J; Ollier S; Davies R J. ALLERGY, (1984 Oct) 39 (7) 521-8. Journal code: 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB Hyposensitization with a **tyrosine adsorbed** extract of Dermatophagoides pteronyssinus was effective in relieving symptoms in selected patients with perennial rhinitis due to this **allergen** who had responded poorly to topical application of steroids. There was a significant reduction in the nasal response to **allergen** after six weekly injections only in the actively treated group, but symptomatic improvement greater than that produced by placebo therapy was only evident after a further 10 months of monthly injections. Significantly more placebo-treated patients considered that therapy was ineffective and withdrew from the study. Only one patient developed significant unwanted effects from the injection therapy and had to be withdrawn from the study. We conclude that hyposensitization with a **tyrosine** **adsorbed** extract of Dermatophagoides pteronyssinus can be a safe and effective treatment for adults with perennial rhinitis due to this **allergen** who have responded poorly to nasal corticosteroids, and that those patients who eventually respond clinically are likely to have a diminished nasal response to **allergen** after the first 6 weeks of therapy.

L8 ANSWER 10 OF 40 MEDLINE
82264333 Document Number: 82264333. PubMed ID: 7107028. l-**Tyrosine** as an immunological adjuvant. Wheeler A W; Moran D M; Robins B E; Driscoll A. INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1982) 69 (2) 113-9. Journal code: 0404561. ISSN: 0020-5915. Pub. country: Switzerland. Language: English.

AB A series of experiments has been carried out to investigate the adjuvant properties of the amino acid L-**tyrosine** in laboratory animals. Adsorption of various allergenic materials to L-**tyrosine** was found to enhance the induction of IgG antibodies, but no unusual propensity to stimulate IgE antibody or delayed hypersensitivity was observed. Administration of the amino acid at a site remote from the **allergen** was found not to augment antibody production. This,

together with evidence of reduced bioavailability of the **tyrosine-adsorbed allergen**, suggested that the adjuvant activity observed resulted from a short-term depot effect.

L8 ANSWER 11 OF 40 MEDLINE
82076388 Document Number: 82076388. PubMed ID: 6796618. Clinical and immunologic evaluation of glutaraldehyde-modified **tyrosine-adsorbed** short ragweed extract: a double-blind, placebo-controlled trial. Metzger W J; Dorminey H C; Richerson H B; Weiler J M; Donnelly A; Moran D. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1981 Dec) 68 (6) 442-8. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB Glutaraldehyde-modified, **tyrosine-adsorbed** ragweed extract (GTR) is a modification of **allergen** extract to reduce allergenicity but retain immunogenicity. We evaluated the clinical efficacy and immunologic changes associated with the administration of GTR (16,350 protein nitrogen units) or placebo to a group of 100 atopic subjects with ragweed hay fever. The study was carried out in a double-blind, placebo-controlled fashion. Clinical response was measured by daily symptom diaries. physician evaluations, and patient responses. Changes in ragweed-specific IgE and IgG antibody were evaluated with an amplified enzyme-linked immunosorbent assay (alpha-ELISA) and were compared with measurements by RAST and a protein A-binding assay for IgG antibody. Treatment with GTR resulted in a sixfold increase in blocking IgG antibody and a small increase in IgE-specific antibody. No changes occurred in the placebo treated group. Mild immediate local reactions occurred after 74% of injections, and late-onset local reactions occurred after 62% of injections in the treated group. The placebo-treated group experienced immediate or late local reaction after only 12% of injections. There were two mild late-onset urticarial reactions of a generalized nature in the treatment group. The treatment group experienced significantly fewer symptoms than the placebo group throughout the season (p less than 0.02), although the difference was not dramatic. The results showed that GTR could be safely given in five preseasonal injections, with retained immunogenicity but less potential for generalized reactions. GTR is an improved method of allergy immunotherapy with the potential for clinical benefit when used in a brief preseasonal treatment regimen.

L8 ANSWER 12 OF 40 MEDLINE
81229065 Document Number: 81229065. PubMed ID: 6166163. Influence of preseasonal treatment with L-**tyrosine-adsorbed** allergoids on IgE-mediated histamine release from basophils of children suffering from allergic diseases. Wegner F; Fenkes A; Stemmann E A; Reinhardt D. AGENTS AND ACTIONS, (1981 Apr) 11 (1-2) 111-3. Journal code: 0213341. ISSN: 0065-4299. Pub. country: Switzerland. Language: English.
AB In 10 children suffering from allergic pollinosis and/or asthma, a preseasonal hyposensitization scheme with 3 weekly injections of a glutaraldehyde-modified, **tyrosine-adsorbed** grass-pollen **allergen** reduced the histamine release from basophils in response to increasing concentrations of antigen. The decrease in histamine release which occurred 1 week after the injection course was even maintained during the pollen season. The inhibition was only obtained when basophils were incubated with the serum of patients, but not with the serum of normals, indicating that blocking antibodies may have occurred. In contrast to what has been observed in the treated patients' group, 5 patients, who were not included in the hyposensitization scheme, showed identical histamine release curves during the whole investigation period. Specific IgE did not increase after the treatment course and shows the same behaviour as the untreated patients. Thus, as treatment with glutaraldehyde modified, **tyrosine-adsorbed** allergoids is safe to administer, requires only 3 injections, reduces histamine release from basophils by production of "blocking" antibodies, it appears to be a useful tool in the

hyposensitization treatment.

L8 ANSWER 13 OF 40 MEDLINE
81207539 Document Number: 81207539. PubMed ID: 7236365. [Research on a new allergenic extract **adsorbed** on L-**tyrosine**. Pharmacological and immunotherapeutic findings]. Ricerche su un nuovo estratto allergenico adsorbito su L-tirosina. Indagini farmacologiche ed immunoterapiche. Vargiu G; Temelcou O; Tassi G C. BOLLETTINO DELL ISTITUTO SIEROTERAPICO MILANESE, (1980) 59 (6) 646-54. Journal code: 17720040R. ISSN: 0021-2547. Pub. country: Italy. Language: Italian.
AB Antigen-specific immunotherapy, whose usefulness has been widely and objectively documented in the last few years, and whose therapeutic effectiveness depends on the administration of high doses of antigen, exploits the use of retard allergenic extracts which turn out to be more tolerated, and liable to a lower occurrence of side-effects. The Authors describe the results obtained with pollinosis vaccine **adsorbed** on L-**tyrosine** and employed on 206 patients with seasonal allergic conditions. Pharmacological experiments were performed on these vaccines, to establish their general tolerability (on mice and guinea-pigs), their local tolerability and the prolonged tolerability on rats. The results of the pharmacological experiments show that the vaccine does not cause any side-effects or toxic phenomena, that the growth curve of the animals treated is superposable to that of the controls, and that the product is perfectly absorbed without irritation or phlogosis of the peripheral tissues. As far as the clinical data are concerned a high percentage of cases (56.6%) classified as "optimal" were observed, while only a low percentage (4.54%) showed results classified as "null". Concerning the occurrence and the frequency of side-effects we should like to point out that only in one of the 206 cases tested (0.48%) was there local itching. These data are particularly significant, when compared with the side effects registered during immunotherapy with the aqueous vaccines.

L8 ANSWER 14 OF 40 MEDLINE
81055076 Document Number: 81055076. PubMed ID: 7001494. Leucocyte migration inhibition test results during desensitization treatment of children with atopic asthma. Sychlowy A. PHARMATHERAPEUTICA, (1980) 2 (6) 397-400. Journal code: 7606274. ISSN: 0308-051X. Pub. country: ENGLAND: United Kingdom. Language: English.
AB A study was carried out in 16 children with perennial allergic asthma to evaluate the use of the leucocyte migration inhibition factor, one of the indicators of cellular change effected by specific antigens, as a measure of the efficacy of desensitization therapy with a **tyrosine-adsorbed** house dust mite vaccine. Eleven of the children showed a good response and 5 a poor response to desensitization. The results of the migration inhibition test suggest that during specific desensitization therapy asthmatic children acquire the ability to inhibit leucocyte migration by a specific **allergen** and this phenomenon appears to be related to an improved response to treatment.

L8 ANSWER 15 OF 40 MEDLINE
79071967 Document Number: 79071967. PubMed ID: 723401. [New possibilities of hyposensitization with pollen-l-**tyrosine** complexes (author's transl)]. Neue Hyposensibilisierungsmoglichkeiten mit Pollen-L-Tyrosinkomplexen. Horak F. LARYNGOLOGIE, RHINOLOGIE, OTOLOGIE, (1978 Nov) 57 (11) 961-5. Journal code: 7513628. ISSN: 0340-1588. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: German.
AB The so far most comprehensive individual study into the clinical findings in the hyposensitization therapy with pollen-L-**tyrosine** complexes in 253 pollinosis patients, who were first subjected to a hyposensitization therapy, permitted a comprehensive evaluation of the indication possibilities of these preparations (Pollagen, Tyrosin-Allergoid; in other countries available as Pollinex, Polvac,

Bencard-Polen). The success of this hyposensitization, which may be reduced to three injections, can be immunologically established and is only slightly smaller than in the case of a specific desensitization over a period of 5--6 months preseasonally. The therapy is indicated first and foremost in patients who either have a moderate or medium-degree sensitization to grass pollens or who come to a medical examination only briefly before the pollen season. The addition of rye pollens obviously gives the preparation Tyrosin-Allergoid an advantage over the mixture of pure grass pollens as used in Pollagen. Rye pollens are responsible for the highest pollen concentrations and thus for the most severe complaints of pollinosis patients. A considerable increase in the therapeutic success, approximately 20%, can be achieved on the basis of a therapy modification, presented here for the first time: The patient is treated preseasonally with a specific desensitization vaccine and immediately before the pollen season he is additionally vaccinated with **tyrosine-adsorbed** pollen **allergens** as a kind of booster vaccination.

L8 ANSWER 16 OF 40 MEDLINE

75209599 Document Number: 75209599. PubMed ID: 238873. Standardization of Dermatophagoides pteronyssinus extracts and **tyrosine** adsorbates. Dewdney J M; Hordle D A; Munro A C; Shah C. DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1975) 29 378-88. Journal code: 0427140. ISSN: 0301-5149. Pub. country: Switzerland. Language: English.

AB Human skin test, inhibition of RAST and the radioimmunosorbent technique of Ceska have been shown to be useful assays for the standardization of D. pteronyssinus aqueous extracts. The development of these assay systems for the standardization of D. pteronyssinus **tyrosine adsorbed** formulations is described. **Tyrosine** solubilisation procedures are detailed together with the influence of these procedures on the three assays. Good correlation has been shown between the human skin test and the radioimmunosorbent technique. The inhibition of RAST appears to be more sensitive than the other techniques to mild conformational changes in the **allergen**, induced in this work by acid pH. This may limit its value for the standardization of D. pteronyssinus **tyrosine** adsorbates but it may prove useful in monitoring manufacturing processes.

L8 ANSWER 17 OF 40 MEDLINE

75209598 Document Number: 75209598. PubMed ID: 1149941. A radioimmunoassay for chemically modified grass pollen **allergen**. Hordle D A; Munro A C; Newland B J. DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1975) 29 370-7. Journal code: 0427140. ISSN: 0301-5149. Pub. country: Switzerland. Language: English.

AB Because of the physicochemical properties of **tyrosine adsorbed** chemically modified grass pollen **allergens** neither the human skin test in atopic volunteers nor the inhibition of the radioallergosorbent test are suitable assay procedures. Radioimmunoassays involving a labelled IgG fraction of rabbit antisera to the modified materials can be developed. The dilution inherent in the solubilisation procedure for the **tyrosine** does not, in most cases, take the antigen concentration below the level of sensitivity of the assay. Assay of different batches of Pollinex with an inhibition assay shows that discernment of different dose levels is possible. The results are compared with a method of assaying total protein.

L8 ANSWER 18 OF 40 MEDLINE

75072782 Document Number: 75072782. PubMed ID: 4613367. A trial of house dust mite **adsorbed** on **tyrosine** in general practice. Lees L J. BRITISH JOURNAL OF CLINICAL PRACTICE, (1974 Oct) 28 (10) 343-46. Journal code: 0372546. ISSN: 0007-0947. Pub. country: ENGLAND: United Kingdom. Language: English.

L8 ANSWER 19 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001370689 EMBASE Standardisation of a glutaraldehyde-modified **allergen tyrosine adsorbed** vaccine using an assay system with a europium label. Newland B.J.; Lees B.G.; Woroniecki S.R.. S.R. Woroniecki, Allergy Therapeutics Ltd., Dominion Way, West Sussex BN14 8SA, United Kingdom. stefan.woroniecki@allergytherapeutics.com . International Review of Allergology and Clinical Immunology 7/3 (95-101) 2001.
Refs: 12.
ISSN: 1232-9142. CODEN: IRAIFY. Pub. Country: Poland. Language: English. Summary Language: English; Polish.

AB A novel immunometric assay has been developed for the measurement of the antigenic potency of an allergy vaccine formulated with a chemically modified tree pollen extract. In this assay, native or glutaraldehyde-modified tree pollen extract is **adsorbed** onto a microtitre plate well and then reacted with specific rabbit antiserum. Europium-labelled staphylococcal protein A (SPA) is added to bind to the antibody:antigen complex, the uptake of which is directly related to the initial antigen concentration. Europium ligand is preferentially liberated from the SPA by addition of an acid solution and quantification is provided by time resolved fluorescence. The employment of europium, a lanthanide label, offers increased sensitivity when compared to an enzyme/ substrate tagging system, and results in a safer and more environmentally friendly alternative to radioimmunoassay. The europium based analysis shows good correlation with an existing radioimmunoassay, providing a validated assay system for use in product release. This enables standardisation of the therapeutic vaccine for Quality Control (QC) purposes and registration of the product.

L8 ANSWER 20 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001009802 EMBASE Immunotherapy in atopic dermatitis. Mastrandrea F.. F. Mastrandrea, Allergy/Clinical Immunology Centre, A.O.S.S. Annunziata, via Bruno, 74100 Taranto, Italy. Fulvio17@interfree.it. Expert Opinion on Investigational Drugs 10/1 (49-63) 2001.
Refs: 144.
ISSN: 1354-3784. CODEN: EOIDER. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Atopic dermatitis (AD) is a common inflammatory disease involving the skin and often other organs and systems, mainly respiratory. A definitive general consensus on the AD pathogenesis has not yet been established, however several lines of evidence suggest that T-cells play a crucial role in priming AD early-stage lesions. Main topics involved in the disease pathogenesis have been reviewed, which considered the concept of local and systemic haemopoietic events as important contributors to allergic inflammation, a concept now achieving great acceptance. The recently recognised atopic nature of the skin inflammation in AD has raised increasing interest for treatment with **allergen**-specific immunotherapy. However, we only found eight studies using specific immunotherapy (SIT) in AD, two double-blind, placebo-controlled (DBPC) and six observational. One controlled and five observational reported favourable outcomes. The one unique study providing negative results was flawed by the ineffective oral route of extract administration. Despite being encouraging, the reported results do not allow definitive conclusions based on meta-analytic techniques because the amount and quality of information in the literature is not sufficient. The highly promising sub-lingual immunotherapy (SLIT) is discussed with its potential capability of controlling not only the skin lesion severity but also its capability of preventing the development of atopic dermatitis into asthma.

L8 ANSWER 21 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000202519 EMBASE [Standardisation of **tyrosine-adsorbed** glutaraldehyde - Modified grass pollen extract (Pollinex.RTM. Grass)]. STANDARDIZACIA EXTRAKTOV TRAVNYCH PEL'OV ADSORBOVANYCH NA TYROZIN A

MODIFIKOVANYCH GLUTARALDEHYDOM (POLLINEX.RTM. GRASS). Wheeler A.W.; Lees B.. A.W. Wheeler, Allergy Therapeutics Ltd., Dominion Way, Worthing, West Sussex BN14 8SA, United Kingdom. Klinicka Imunologia a Alergologia 10/1 (38-42) 2000.
Refs: 6.
ISSN: 1335-0013. CODEN: KIALEZ. Pub. Country: Slovakia. Language: Slovak. Summary Language: English; Slovak.

AB **Allergen** immunotherapy using a standardised modified **allergen** extracts has been used for successful treatment of type I allergy for many years. All constituents of allergy vaccines are subject of analysis to improve the standardisation of vaccines over last decade. Method of new approaches for this shows this impartion.

L8 ANSWER 22 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

90241274 EMBASE Document No.: 1990241274. Clinical efficiency of hyposenitization with tryosine-**adsorbed**, glutaraldehyde modified dermatophagoides pteronyssinus antigen in respiratory allergy. Sirianni M.C.; Tagliaferri F.; Di Sabatino A.; Bonomo R.. Department of Allergy and Clinical Immunology, University La Sapienza of Rome, Italy. Perspectives in E.N.T. - Immunology 3/2 (159-163) 1989.
ISSN: 1120-2556. CODEN: PEEIE5. Pub. Country: Italy. Language: English. Summary Language: English.

AB The clinical efficiency of hyposensitization with a **tyrosine-adsorbed**, glutaraldehyde modified Dermatophagoides pteronyssinus (DPT) antigen (Bencard DP6) was evaluated after different periods of treatment in thirty patients suffering from allergic rhinitis or bronchial asthma. Atopy to this **allergen** was confirmed on the basis of clinical history and skin prick tests. In some patients with bronchial asthma peak espiratory flow rate was also measured to confirm the diagnosis. Clinical efficiency of hyposensitization with Bencard DP6 was evaluated on the basis of the relief of symptoms after periods of treatment ranging from 1-4 years. Our results show an improvement of the symptoms, both in rhinitis and in bronchial asthma, even after a one-year treatment period.

L8 ANSWER 23 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

83025228 EMBASE Document No.: 1983025228. Cellular and humoral responses following one year of hyposensitization with aqueous and **tyrosine adsorbed** Dermatophagoides pteronyssinus extracts. Hanneuse Y.; Pintens H.; Delespesse G.. Dep. ORL, Hop. Univ. St. Pierre, Brussels Free Univ., Brussels, Belgium. Allergologia et Immunopathologia 10/4 (289-294) 1982.
CODEN: AGIMBJ. Pub. Country: Spain. Language: English. Summary Language: Spanish.

L8 ANSWER 24 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

82138853 EMBASE Document No.: 1982138853. [Experiences with an L-**tyrosine adsorbed** extract of the house dust mite D. pteronyssinus in the treatment of mite sensitive patients]. ERFAHRUNGEN MIT EINEM AN L-TYROSIN ADSORBIERTEN EXTRAKT DER HAUSSTAUBMILBE D. PTERONYSSINUS BEI DER BEHANDLUNG MILBENALLERGISCHER PATIENTEN. Deichmann B.; Schreyer H.. Vossstr. 57, D-4180 Goch, Germany. Allergologie 5/1 (11-18) 1982.
CODEN: ALLRDI. Pub. Country: Germany. Language: German. Summary Language: English.

AB 36 Patients with allergic rhinitis and/or bronchial asthma have been treated in a dermatologic practice with an L-**Tyrosine adsorbed** extract of the house dust mite Dermatophagoides pteronyssinus (Tyrivac = Migen). The vaccine was shown to be very well tolerated and extraordinary effective. A clear correlation between the duration of treatment and efficacy was observed. Termination already during the basic course lead to failure of improvement. The importance of an exact diagnostic procedure became evident.

L8 ANSWER 25 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
81062207 EMBASE Document No.: 1981062207. Influence of hyposensitization therapy on clinical and immunological parameters in asthma and rhinitis patients. Comparative study of a **tyrosine adsorbed** house dust mite vaccine (H.D.M.) and an aqueous H.D.M. vaccine. Hanneuse Y.; Pintens H.; Delespesse G.. Univ. Hosp. St Pierre, Brussels, Belgium. Allergologia et Immunopathologia 8/4 (350-351) 1980.
CODEN: AGIMBJ. Pub. Country: Spain. Language: English.

L8 ANSWER 26 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
81028659 EMBASE Document No.: 1981028659. Immunotherapy with **tyrosine -adsorbed** vaccine of house dust mite in respiratory allergies. Kang S.Y.; Moon H.B.; Ro Y.-M.. Dept. Int. Med., Coll. Med., Seoul Nat. Univ., Seoul, Korea, Republic of. Seoul Journal of Medicine 21/2 (179-186) 1980.
CODEN: SUICAC. Pub. Country: Korea, Republic of. Language: Korean. Summary Language: English.
AB House dust mites (HDM), as major antigens in house dust, is one of the most important offending **allergens** in bronchial asthma and allergic rhinitis. In Korea, Cho et al. found Dermatophagoides farinae (53.6%) and D. pteronyssinus in house dust, which are the main species of house dust mites responsible for respiratory allergy in many countries. Kang et al. reported that 26% of respiratory allergic patient in Korea have positive skin reaction to the extract of D. pteronyssinus in prick test. Because the avoidance of house dust mites is practically impossible, the hyposensitization treatment (immunotherapy) may be the only effective radical treatment. To evaluate the efficacy of the hyposensitization treatment in HDM sensitized respiratory allergies, we tried it on 35 patients (18 bronchial asthma patients, 8 allergic rhinitis patients and 9 combined cases) with a **tyrosine-adsorbed** glycerinated extract of D. pteronyssinus, and the following results were obtained. As a whole, the efficacy of the treatment was substantial in 10 patients (28.6%) and fair in 17 patients (48.6%), so about 77% of the studied subjects had significant symptomatic reliefs. In relation to the disease entity, the efficacy of the treatment was substantial in 6 of 18 bronchial asthma patients and in 2 allergic rhinitis patients. The shorter the duration of the disease is, the more excellent the efficacy of treatment resulted. If the duration was less than 1 year, 40% of the patients had a substantial effect, and if it was more than 11 years, the patients go no such effect. Almost all of the patients with a substantial effect were below 30 yr of age, indicating a better effect in younger age. A seasonal relationship of the symptom and sex difference had no significant relationship with the efficacy of the treatment.

L8 ANSWER 27 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
81015187 EMBASE Document No.: 1981015187. [Results of a multicenter-study on the hyposensitization of pollinosis patients with a tyrosin-**adsorbed** grass- and rye pollen extract (TA tyrosin-allergoid-Graserpollen)]. ERGEBNISSE EINER MULTICENTERSTUDIE ZUR HYPOSENSIBILISIERUNG VON POLLINOSIS-PATIENTEN MIT EINEM TYROSIN-ADSORBIERTEN GRASER-UND ROGGENPOLLENEXTRAKT (TA TYROSIN-ALLERGOID-GRASERPOLLEN). Schreyer H.. Dept. Klin. Forsch. Allergie Johann A.Wulfing 4040 Neuss, Germany. Allergologie 3/2 (92-100) 1980.
CODEN: ALLRDI. Pub. Country: Germany. Language: German. Summary Language: English.
AB 203 Pollinosis patients aged 4 to 60 yr have been treated 1978 preseasonally with the **tyrosine**-adsorbate TA Tyrosin-Allergoid-Graserpollen (Bencard) at ten allergological centers. The notes of 179 patients were complete and could be evaluated and differentiated between conjunctivitis (n = 168), rhinitis (n = 177) and bronchial asthma (n = 89). Conjunctivitis improved in 67.8%, rhinitis in 74.0% and asthma only in 46.1%. Some plausible explanations for the

relatively poor results in the case of asthma are discussed. Local side effects, usually of mild to moderate nature, occurred with a similar incidence as after injections of alum-**adsorbed allergen** extracts. Systemic reactions have been caused by injections of the **tyrosine**-adsorbate with a much lower incidence than by injections of traditional 'vaccines'. Usually they were described as exacerbations of typical hay fever symptoms. No patient developed a severe generalized reaction, especially no anaphylactic shock or a threatening bronchospasm.

L8 ANSWER 28 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
79038583 EMBASE Document No.: 1979038583. Results of a clinical trial with a Dermatophagoides pteronyssinus **tyrosine adsorbed** vaccine. Amaral Marques R.; Avila R.. Serv. Doencas Pulmon., Fac. Med., Hosp. Santa Maria, Lisboa, Portugal. Allergologia et Immunopathologia 6/3 (231-235) 1978.
CODEN: AGIMBJ. Pub. Country: Spain. Language: English. Summary Language: Spanish.
AB Twenty-eight patients were included in a double-blind placebo-controlled study of a vaccine containing **tyrosine-adsorbed** Dermatophagoides pteroyssinus antigen (Migen(R)). The aim of the trial was to show the efficacy and safety of Migen as a 6-injection course, with or without a follow-up course of 6 maintenance doses, for the treatment of bronchial asthma. The patients selected had suffered from perennial asthma for at least 2 years and gave a strong skin reaction to house dust mite. The subjects in the study were divided into two groups: twelve patients receiving only a standard course of six graded injections at weekly intervals and another group of sixteen patients receiving the same course followed by a maintenance course comprising six injections of the highest strength (400 N.U.). Approximately half the patients in each of these groups were on placebo. Assessment was based on the patient's and doctor's impression of the response to the treatment using a daily symptom record card and clinical observation of the patient at regular intervals. The overall assessment was graded in accordance with the following four point scale: very good, good, same and worse. The results showed that the patients receiving Migen as a 6-injection course responded better than patients receiving placebo; moreover, patients who received 6 maintenance injections of Migen gave a very good or good response compared to those who were submitted to 12 injections of placebo and also compared to those receiving the standard course. Particular notice was taken of the side effects of the vaccine. Migen proved to be a good and safe method of treating bronchial asthma due to house dust mite.

L8 ANSWER 29 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
78395836 EMBASE Document No.: 1978395836. [House dust allergies treated with a house dust mite vaccine **adsorbed** on **tyrosine**]. BEHANDLUNG VON HAUSSTAUBALLERGIEN MIT EINER AN TYROSIN ADSORBIERTEN HAUSSTAUBMILBEN-VAKZINE. Czarnecki N.. Univ. Klin. Dermatol. Venerol., Innsbruck, Austria. H+G Zeitschrift fur Hautkrankheiten 53/15 (543-547) 1978.
CODEN: ZHKRAJ. Pub. Country: Germany. Language: German. Summary Language: English.
AB Desensitization treatment of house dust allergies with L-**Tyrosine adsorbed** house dust mite vaccine is described. It is stressed that the success of the treatment depends on an exact diagnosis and sufficiently long treatment period.

L8 ANSWER 30 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
78133352 EMBASE Document No.: 1978133352. [Allergoids bound to **tyrosine**]. L TYROSIN GEBUNDENE ALLERGOIDE. Overell B.G.. Beecham Pharmaceut., Res. Div., Betchworth, United Kingdom. Therapiewoche 27/22 (4325-4331) 1977.
CODEN: THEWA6. Pub. Country: Germany. Language: German.
AB Grass pollen extracts were produced in a particular way such that they

were given preliminary treatment with glutaraldehyde, and **adsorbed** in an L **tyrosine** suspension. After treatment with glutaraldehyde, the capacity of Timothy pollen extract to react with human allergic antibodies was reduced, but the capacity to induce IgG was not affected. Adsorption with **tyrosine** produces a depot formulation with an increased immunity reaction.

L8 ANSWER 31 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:155443 Document No.: PREV200000155443. Standardisation of glutaraldehyde-modified **allergen tyrosine**-**adsorbed** vaccines using an assay system with a Europium label. Newland, B. (1); Lees, B. G. (1); Wheeler, A. W. (1). (1) Allergy Therapeutics Ltd., Worthing, BN14 8SA UK. Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 144. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology. ISSN: 0019-2805. Language: English. Summary Language: English.

L8 ANSWER 32 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:155433 Document No.: PREV200000155433. Standardisation of glutaraldehyde-modified **allergen tyrosine**-**adsorbed** vaccines containing the TH-1-inducing adjuvant, MPL. Hopkins, M. (1); Lees, B. G. (1); Richardson, D. W. G. (1); Wheeler, A. W. (1). (1) Allergy Therapeutics Ltd., Worthing, BN14 8SA UK. Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 141. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology. ISSN: 0019-2805. Language: English. Summary Language: English.

L8 ANSWER 33 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1991:313676 Document No.: BA92:24191. STANDARDIZATION OF GLUTARALDEHYDE-MODIFIED **TYROSINE-ADSORBED ALLERGEN** EXTRACTS. OVERELL B G; SPACKMAN D A; WHEELER A W; PFEIFER P. STRESEMANNALLEE 6, W-4040 NEUSS 1.. ALLERGOLOGIE, (1991) 14 (3), 110-115. CODEN: ALLRDI. ISSN: 0344-5062. Language: German.
AB A new assessment of the allergoid properties of glutaraldehyde-modified grass pollen extract has been made in order to validate standardization procedures. Increasing substitution of amino groups with glutaraldehyde led to a loss of allergenicity of extracts, as measured by RAST inhibition and by histamine release from sensitized human basophils. Both modified and unmodified materials induced IgG antibody in guinea-pigs. The antibody-stimulating capacity of the modified matrials could not be accounted for by the presence of unmodified activity in the modified samples. The antibodies induced by modified materials had a spectrum of specificities similar to that induced by unmodified extract, these specificities appearing to be directed at allergenic components when assessed by SDS-PAGE immunoblotting. One such specificity was to a major **allergen** component R7 (Lol p I) of temperate grass pollen. Since immunoreactivity with rabbit IgG antibody specific for R7 was retained in all the modified samples, a basis for an assay for standardization of glutaraldehyde-modified **allergen** products was established. The rationale for the use of this assay, and its use in establishing "standardized unit" system is explained.

L8 ANSWER 34 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1989:248655 Document No.: BA87:129720. FIRST RESULTS OF A MULTICENTER TRIAL FOR SPECIFIC IMMUNOTHERAPY USING **TYROSINE ADSORBED** EXTRACTS TYROSIN S. RENNER B; DRACHENBERG K J. STRESEMANNALLEE 6, D-4040 NEUSS 1.. ALLERGOLOGIE, (1989) 12 (1), 27-35. CODEN: ALLRDI. ISSN: 0344-5062. Language: German.
AB The new developed depot preparation Tyrosin S for specific immunotherapy

has been used for treatment of 240 patients in a multicenter study carried out at 15 centers in Germany. Tyrosin S contains patient-specific mixtures of **tyrosine adsorbed allergen** extracts. In 74 out of 100 patients (group 1) efficacy and safety of immunotherapy with Tyrosin S could be assessed. In 112 out of 140 patients (group 2) additional safety data were generated. For most patients symptom improvement and safety was evaluated after one single treatment course given pre-seasonally (pollen allergic patients) or for one year (house dust mite allergic patients). All patients with previous hyposensitization treatment were excluded as well as asthmatics on systemic high dose corticosteroid therapy. Efficacy (group 1)-based on change in and duration of symptoms-was shown by a good to very good beneficial effect of treatment in 85% of all patients (90% of house dust mite allergic patients). In 77% of patients a marked reduction of antiallergic drug consumption was found. The level of **allergen**-specific IgG serum antibodies in random samples of grass pollen allergic patients increased significantly ($p < 0.05$), those of house dust mite allergic patients only marginally. However, no correlation between the IgG response and the clinical outcome could be shown. Based on the rate of local (11.6%) and systemic (1.08%) reactions in 21,2 patients tolerance of Tyrosin S was found to be comparable to that of other preparations (e.g. ADL).

L8 ANSWER 35 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1987:333592 Document No.: BA84:42535. HYPOSENSITIZATION AGAINST POLLENS DURING THE ENTIRE YEAR OR PRESEASONAL. ZIMMERMANN T; PETZENHAUSER C. LOSCHGESTRASSE 15, D-8520 ERLANGEN.. ALLERGOLOGIE, (1987) 10 (5), 183-187. CODEN: ALLRDI. ISSN: 0344-5062. Language: German.

AB 211 children with sensitization against pollens have been observed over a period of 3 years. The diagnosis was done by the history and the skin prick test. The solution for the hypersensitization was additionally composed on the base of the actuality of different pollenallergens. We used a semi-depot extract solution containing 1-4 different pollen **allergens** for the therapy during the entire year. Within the pollen season, we reduced the dose (a quater from the previous dose) and gave this weekly by s.c. injections. 87% from 104 children with pollen allergy showed a good improvement of pollinosis and asthma. 56 children were treated preseasonal by 3 injections of an allergoid **adsorbed** to L-**tyrosine**, containing grasspollens and cultivated ryepollen. 57% of these children showed improvement of pollinosis and pollen asthma. Another group of 59 children was only treated by antiallergic drugs (DNCG, Ketotifen, Antihistamines, Corticosteroids). 59% of these children had better results. There was an increase of the therapeutic effect within a period of three years in the children with hyposensitization. We saw good therapeutic effects especially in pollen asthma. In 16-18% we saw side effects such as weariness, itch, headache rhinitis, infiltration of the skin after injection and asthma. There was no increase in the side effects during the pollen season. Because of the improvement of pollen asthma, we suggest, that children suffering from pollen asthma should be treated continuously by hyposensitization without regard to the pollen season.

L8 ANSWER 36 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1985:366823 Document No.: BA80:36815. INCREASE OF SPECIFIC IMMUNOGLOBULIN ANTIBODIES IN SPECIFIC IMMUNOTHERAPY DOUBLE-BLIND CONTROLLED TRIAL IN GRASS POLLEN ALLERGY. PASTORELLO E; JOPPOLO G; FIOCCHI A; SILLANO V. ISTITUTO DI CLINICA MEDICA II, UNIVERSITA DI MILANO.. FOLIA ALLERGOL IMMUNOL CLIN, (1984 (RECD 1985)) 31 (5), 353-360. CODEN: FAICAZ. ISSN: 0303-8432. Language: Italian.

AB Fifteen grass pollen sensitive asthmatic patients underwent a double blind trial of specific immunotherapy [ITS] with a mixture of 3 grass pollen aqueous extracts (Holcus lanatus, Anthoxanthum odoratum and Phleum pratense) or placebo. After 10 mo. the mean maintenance dose of pollen extract in 8 actively treated patients was 6,000 RAST [radioallergosorbent technique U] (range 3,000-8,000) and the mean total dose was 18.70 RAST U

(range 10,200-30,000). There was a significant difference between the mean symptoms score values of treated patients vs. controls (2.4 vs. 7.0 P < 0.001). No significant differences or changes in IgE Ab to timothy in serum and nasal secretions were found in the 2 groups before or after ITS total IgG and all 4 IgG Ab subclasses to Timothy antigen D increased significantly in actively treated patients (P < 0.005 for each). The increase in IgG4 subclass Ab, however, was greater than that of the other 3 IgG subclasses (P < 0.05). In a further experience 22 children were studied before and after preseasonal ITS with 3 doses of grass pollen extract **adsorbed** with **tyrosine**. Clinical improvement was mild and there was not a significant difference in specific IgG before an after treatment. Clinical efficacy of ITS apparently is correlated to the increase of IgG Ab to the **allergens**.

L8 ANSWER 37 OF 40 SCISEARCH COPYRIGHT 2002 ISI (R)

92:302325 The Genuine Article (R) Number: HT084. A DOUBLE-BLIND CONTROLLED TRIAL OF HYPOSENSITIZATION TO DERMATOPHAGOIDES-PTERONYSSINUS IN CHILDREN WITH ATOPIC ECZEMA. GLOVER M T (Reprint); ATHERTON D J. HOSP SICK CHILDREN, LONDON WC1N 3JH, ENGLAND. CLINICAL AND EXPERIMENTAL ALLERGY (APR 1992) Vol. 22, No. 4, pp. 440-446. ISSN: 0954-7894. Pub. country: ENGLAND. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A double-blind controlled trial of hyposensitization with **tyrosine-adsorbed** Dermatophagoides pteronyssinus vaccine in 24 children with atopic eczema and immediate hypersensitivity to D. pteronyssinus failed to demonstrate superiority over placebo after a standard 8 month course of treatment.

In a second phase, children initially administered active treatment were randomly allocated to continue with active treatment or switched to placebo for a further 6 months. The clinical scores suggest that prolonged hyposensitization may be more effective than placebo but the numbers were too small to permit confident conclusions. A dramatic placebo effect may have served to conceal any additional therapeutic effect from active treatment.

L8 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2002 ACS

1991:214429 Document No. 114:214429 Multiphasic sustained-release injectable containing microencapsulated biomacromolecular agents. Silvestri, Louis J.; Pyle, Ruth H. (Biosearch, Inc., USA). PCT Int. Appl. WO 9009166 A1 19900823, 26 pp. DESIGNATED STATES: W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU; RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1990-US750 19900208. PRIORITY: US 1989-301453 19890124.

AB A multiphasic sustained release injectable delivery system is provided, as well as a method for treating humans and other mammals with that multiphasic sustained release system. The multiphasic sustained release system comprises prolonged, controlled delivery of microencapsulated biomacromol. agent of biol. origin comprising the bioactive agent encapsulated in microcapsules of bioerodible encapsulating polymer, which permits a sustained, multiphasic release of said bioactive agent, including (i) a 1st portion of said bioactive agent that upon injection is capable of being released from said microcapsules of bioerodible encapsulating polymer in a manner whereby only a relatively small amt. of said bioactive agent is related during said 1st phase, whereby initial biol. reaction is minimized due to said first portion producing a mild reaction similar to that normally obsd. with low doses of conventional administration; and (ii) 2nd portions of said bioactive agent that provide a substantially higher level of bioactive agent in doses which could provoke a serious reaction in the patient, but for the prior release of said 1st portion. The dosage form is useful for delivery of **allergen** exts., cytokines, etc. Thus, a lactogeneous microcapsule compn. was prepd. contg. an aq. ext. (microspheres) of ragweed (Ambrosia artemisifolia) and lactide-glycolide copolymer. Size of the microspheres

was 5-400 .mu.m. Compns. contg. other **allergens** or contg. .alpha.-interferon are also described.

L8 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2002 ACS
1983:95680 Document No. 98:95680 Pharmaceutical compositions and their use in the therapy of allergic humans. Overell, Brian George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 64366 A1 19821110, 12 pp. DESIGNATED STATES: R: BE, CH, DE, FR, GB, IT, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1982-302077 19820423. PRIORITY: GB 1981-13209 19810429.
AB Compns. contg. noninfective **allergens** and C10-22 alkyl esters of **tyrosine** or their salts as adjuvants are useful for the densensitization of humans allergic to noninfective **allergens**. The compns. may be used in the form of suspensions or solns. as vaccines. Thus, 1-octadecanol [112-92-5] was esterified with L-**tyrosine** [60-18-4] in the presence of dry HCl gas to yield octadecyl L-tyrosinate-HCl [77229-76-6]. This was then neutralized with dil. aq. NaOH soln. and the aq. soln. extd. with ether to give octadecyl L-tyrosinate (I) [73393-27-8]. Rye grass pollen ext. (1 mg) was **adsorbed** on I (40 mg) in a phosphate buffered saline soln. (1 mL). Guinea pigs were s.c. injected with 1 mL of this prepn. and sera prepd. on days 14 and 27 were tested for the presence of ryegrass pollen ext.-specific hemagglutinating antibodies. I was more effective than **tyrosine** itself and nontoxic.

L8 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2002 ACS
1977:527586 Document No. 87:127586 L-**Tyrosine** bound **allergens**. Overell, B. G. (Res. Div., Beecham Pharm., Betchworth/Surrey, Engl.). Therapiewoche, 27(22), 4325, 4328, 4331 (German) 1977. CODEN: THEWA6.
AB Grass pollen exts. were pretreated with glutaraldehyde [111-30-8] and **adsorbed** by a L-**tyrosine** [60-18-4] suspension. After glutaraldehyde treatment, the ability of timothy pollen ext. to react with human allergic antibodies was inhibited, but its ability to induce IgG was retained. Adsorption with **tyrosine** produced a depot formulation with an improved immune reaction.

=> s l2 and "3-DMPL"
L10 1 L2 AND "3-DMPL"

=> d l10 cbib abs

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
1998:682305 Document No. 129:321186 **Allergen** formulations containing tyrosine and deacetylated monophosphorylated lipid A. Ulrich, Jorj Terry; Wheeler, Alan Worland (Smithkline Beecham Plc, UK). PCT Int. Appl. WO 9844947 A1 19981015, 11 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-EP2138 19980403. PRIORITY: GB 1997-6957 19970405.
AB A pharmaceutical compn. comprises tyrosine, an optionally **modified allergen**, and **3-DMPL** (3-de-O-acylated lipid A monophosphorylated), is useful in the prevention and treatment of allergy. Thus, a 0.5 mg/mL grass pollen ext. was **modified** by treatment with 0.25% glutaraldehyde. A pH 7 phosphate buffer was added and the **allergen** soln. was copptd. with tyrosine by the simultaneous addn. of L-tyrosine and 3.2M NaOH. A DPPC soln. was mixed with **3-DMPL** and combine with tyrosine.

```
=> s (ulrich j?/au or wheeler a?/au)
L11       3587 (ULRICH J?/AU OR WHEELER A?/AU)

=> s l11 and tyrosine
L12         78 L11 AND TYROSINE

=> s l12 adn absorbed
MISSING OPERATOR L12 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l12 and adsorbed
L13         40 L12 AND ADSORBED

=> dup remove l13
PROCESSING COMPLETED FOR L13
L14          18 DUP REMOVE L13 (22 DUPLICATES REMOVED)

=> d l14 1-18 cbib abs

L14  ANSWER 1 OF 18  EMBASE  COPYRIGHT 2002 ELSEVIER SCI. B.V.
2002145912  EMBASE  A Th1 inducing adjuvant, MPL.RTM., safely assists in
     reducing the length of a pollen allergy vaccination course. Drachenberg
     K.J.; Wheeler A.W.; Woroniecki S.R.; Horak F.. Dr. S.R.
     Woroniecki, Allergy Therapeutics Ltd, Dominion Way, Worthing, West Sussex
     BN14 854, United Kingdom. Stefan.Woroniecki@allergytherapeutics.com.
     Alergologia e Inmunologia Clinica  17/1 (39-43)  2002.
     Refs: 9.
     ISSN: 1575-734X. CODEN: AICLF4. Pub. Country: Spain. Language: English.
     Summary Language: English; Spanish.
AB   Background and aims: The mechanism of successful allergy vaccination is
     thought to be associated with a promotion of Th1 cell activity. A
     Th1-inducing adjuvant was incorporated in a grass pollen allergy vaccine
     with the aim of improving the efficiency of allergy vaccination such that
     only four injections would be required. Materials and methods: The
     adjuvant, 3-deacylated monophosphoryl lipid A (MPL.RTM., Corixa, USA) was
     formulated in a standardised vaccine employing a tyrosine-
     adsorbed glutaraldehyde-modified grass pollen extract. This new
     therapy was evaluated in a phase III double-blind, placebo-controlled
     study of grass-pollen sensitive patients (81 actively-treated, 60 on
     placebo). Results: Significant improvements were found in nasal (p =
     0.016) and ocular (p = 0.003) symptoms and combined symptom and medication
     scores (p = 0.013). Grass pollen-specific IgG antibody was elevated by
     active treatment (p < 0.01). No seasonal rise in specific IgE was observed
     in the actively-treated group in contrast to the placebo group (p =
     0.002). Local adverse events were higher in the actively-treated group,
     but there were no group differences with generalised adverse events.
     Conclusion: A new grass pollen allergy vaccine incorporating a
     Th1-inducing adjuvant was shown to be well-tolerated and efficacious after
     only four injections. The vaccine is available in a number of countries as
     Pollinex.RTM. Quattro or Quattro MPL.RTM.. This new approach supports the
     use of immunotherapy more widely for the effective treatment of
     specifically diagnosed type 1 allergy. This treatment is now being
     extended to treat allergy to other pollens and to house-dust mites.

L14  ANSWER 2 OF 18      MEDLINE                                  DUPLICATE 1
2001694043  Document Number: 21605984.    PubMed ID: 11738737.    Safety
     evaluation of a glutaraldehyde modified tyrosine
     adsorbed housedust mite extract containing monophosphoryl lipid A
     (MPL) adjuvant: a new allergy vaccine for dust mite allergy. Baldrick P;
     Richardson D; Wheeler A W. (Covance Laboratories Ltd., Otley
```

Road, Harrogate, North Yorkshire HG3 1PY, UK.) VACCINE, (2001 Dec 12) 20 (5-6) 737-43. Journal code: 8406899. ISSN: 0264-410X. Pub. country: England: United Kingdom. Language: English.

AB A new allergy vaccine is currently under clinical evaluation for the prevention or relief of symptoms caused by specific housedust mites. It consists of a 50:50 mixture of the mite Dermatophagoides pteronyssinus and D. farinae protein derived from aqueous extracts of the mites which is chemically modified by glutaraldehyde and **adsorbed** onto L-**tyrosine** with addition of the immunostimulatory adjuvant, monophosphoryl lipid A (MPL) "Polymite". A specific preclinical safety testing strategy was developed to support clinical use and comprised single and repeat dose toxicity, reproduction toxicity and local tolerance studies. Dose levels of up to 0.5ml for the mouse and up to 1ml for both the rat and the rabbit were used. Overall, the product was shown to produce no toxicological findings of significance at levels greatly in excess to those proposed for clinical use. A not unexpected, but relatively minor, immunostimulatory effect was seen following repeated dosing (once weekly for 13 weeks) at 1ml per rat; the Polymite formulation also resulted in injection site reaction which can largely be attributed to the presence of **tyrosine**. No reproduction toxicity was found.

L14 ANSWER 3 OF 18 MEDLINE DUPLICATE 2

2001360896 Document Number: 21314872. PubMed ID: 11421893. A well-tolerated grass pollen-specific allergy vaccine containing a novel adjuvant, monophosphoryl lipid A, reduces allergic symptoms after only four preseasonal injections. Drachenberg K J; **Wheeler A W;** Stuebner P; Horak F. (Bencard Allergie GmbH, Munich, Germany, Allergy Therapeutics Ltd, Dominion Way, Worthing, West Sussex, UK.) ALLERGY, (2001 Jun) 56 (6) 498-505. Journal code: 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB BACKGROUND: We present data showing that a Th1-inducing adjuvant can reduce the number of injections required for allergy vaccination. Allergy vaccination is the only treatment for type 1 hypersensitivity that can alter the underlying disease process. A switch of specific T-cell activity from Th2 >Th1 to Th1 >Th2 is believed to be an important change seen after long-term vaccination therapy. An immunologic adjuvant that enhances such a switch could be used to reduce the number of injections required. This would improve compliance with the treatment and provide pharmacoeconomic advantages. Such an adjuvant is 3-deacylated monophosphoryl lipid A (MPL adjuvant, Corixa). METHODS: A multicentre, placebo-controlled, randomized, double-blind clinical study was performed with a new standardized allergy vaccine comprising a **tyrosine-adsorbed** glutaraldehyde-modified grass pollen extract containing MPL adjuvant. Four subcutaneous injections of the active product were given preseasonally to 81 grass pollen-sensitive subjects, and 60 received placebo injections (**tyrosine** alone). Diary cards were used to record symptoms and medication taken during approximately 30 days of the grass pollen season. RESULTS: There was a statistical advantage in favour of the active treatment for nasal ($P = 0.016$) and ocular ($P = 0.003$) symptoms and combined symptom and medication scores ($P=0.013$). Titrated skin prick testing revealed a significant reduction of skin sensitivity in the active group compared to placebo ($P = 0.04$). Grass-pollen-specific IgG antibody was raised by active treatment ($P < 0.01$). A rise in IgE antibody was seen in the placebo group during the season ($P < 0.01$). The first year's treatment rise of IgE was not seen in the active group, and no rise occurred during the pollen season. More local adverse events were seen in the active group. There was no difference in generalized adverse events. CONCLUSION: A new, well-tolerated allergy vaccine, incorporating a Th1-inducing adjuvant, MPL, was efficacious and after only four preseasonal injections produced antibody changes normally associated with long injection schedules. This may encourage wider application of allergy vaccination. The vaccine is now available in a number of countries as Pollinex Quattro.

L14 ANSWER 4 OF 18 MEDLINE DUPLICATE 3
2002102119 Document Number: 21823094. PubMed ID: 11834183.
Standardisation of glutaraldehyde-modified **tyrosine-adsorbed** tree pollen vaccines containing the Th1-inducing adjuvant, monophosphoryl lipid A (MPL). Hopkins M; Lees B G; Richardson D G; Woroniecki S R; **Wheeler A W.** (Allergy Therapeutics Ltd, West Sussex, UK.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (2001 Nov-Dec) 29 (6) 245-54. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB BACKGROUND: a new range of allergy vaccines has been developed by the introduction of a relatively new Th1-inducing adjuvant known as 3-deacylated monophosphoryl lipid A (MPL). MPL adjuvant is of natural origin, derived from the lipopolysaccharide of Salmonella minnesota R595. This adjuvant is incorporated in a glutaraldehyde-modified pollen extract **adsorbed** to L-**tyrosine** (Pollinex Quattro). A major potential benefit provided by MPL adjuvant is the promotion of a Th1 response which enhances the efficacy of allergy vaccination and can consequently allow a reduction in the number of injections required for treatment. The standardisation of Pollinex Quattro tree pollen allergy vaccine is described and we include details of some innovative analytical procedures. METHODS AND RESULTS: an essential feature of the analytical strategy is the assay of the MPL adjuvant using a recently developed HPLC technique. The adjuvant has a complex chemical structure and the analysis is illustrated in detail. We give a full picture of the vaccine standardisation by describing biochemical and immunological characterisation of the allergen extract, together with some brief manufacturing details. CONCLUSIONS: a high overall level of standardisation is illustrated by a number of different tests applied to all stages of vaccine manufacture. Tree pollen allergen potency is measured following the pollen extraction, chemical modification and formulation as a **tyrosine** adsorbate. Good batch-to-batch reproducibility is shown. The HPLC assay for MPL adjuvant showed high quality resolution which did not vary when measuring raw material or when incorporated in the vaccine and the technically complex assay is shown to be reliable.

L14 ANSWER 5 OF 18 MEDLINE DUPLICATE 4
2001682811 Document Number: 21585804. PubMed ID: 11729351. A Th1-inducing adjuvant, MPL, enhances antibody profiles in experimental animals suggesting it has the potential to improve the efficacy of allergy vaccines. **Wheeler A W;** Marshall J S; **Ulrich J T.** (Allergy Therapeutics Ltd, Worthing, UK.. alan.wheeler@allergytherapeutics.com) . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Oct) 126 (2) 135-9. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Monophosphoryl lipid A (MPL) is a detoxified derivative of the lipopolysaccharide (LPS) moiety of Salmonella minnesota R595, which has retained immunostimulatory activities. MPL has been administered to many subjects in clinical trials as an adjuvant component of infectious disease vaccines and is currently a component of a licensed cancer vaccine, Melacine (Corixa Inc., Schering Plough). MPL has, in particular, been shown to promote Th1-type antigen specific responses. L-**tyrosine** is a depot adjuvant which is fully metabolisable and has been successfully employed in allergy vaccines for a number of years. METHODS: Mice were immunised with MPL adjuvant in conjunction with separate preparations of either ovalbumin or glutaraldehyde-modified ragweed pollen extract both coprecipitated with L-**tyrosine**. The specific antibody isotypes IgG1, IgG2a, IgG2b and also IgE were measured. Rats received booster injections of keyhole limpet haemocyanin (KLH) in conjunction with MPL adjuvant following priming with KLH in alum alone. KLH-specific antibody responses were measured. RESULTS: It was shown that a combination of L-**tyrosine** and MPL were synergistic in enhancing murine antigen

specific IgG antibody responses without enhancing antigen specific IgE responses. Furthermore, this adjuvant combination promoted strong IgG2 antigen specific responses indicative of a Th1 directed response. In KLH sensitised rats, treatment with MPL was shown to prevent a secondary IgE antibody response when injected with booster injections of antigen. CONCLUSIONS: Immunisation of mice with two different antigens **adsorbed** to L-**tyrosine** induced a Th1-skewed primary response when in conjunction with MPL adjuvant which also generally enhances a specific IgG response. Incorporation of MPL adjuvant in the immunisation of rats prevented a secondary specific IgE response. These results suggest that the employment of this new adjuvant in clinical allergy vaccination formulations may result in an improved efficacy which could be utilised in various ways to improve compliance.

L14 ANSWER 6 OF 18 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000202519 EMBASE [Standardisation of **tyrosine-adsorbed** glutaraldehyde - Modified grass pollen extract (Pollinex.RTM. Grass)]. STANDARDIZACIA EXTRAKTOV TRAVNYCH PEL'OV ADSORBOVANYCH NA TYROZIN A MODIFIKOVANYCH GLUTARALDEHYDOM (POLLINEX.RTM. GRASS). **Wheeler A.W.** ; Lees B.. A.W. Wheeler, Allergy Therapeutics Ltd., Dominion Way, Worthing, West Sussex BN14 8SA, United Kingdom. Klinicka Imunologia a Alergologia 10/1 (38-42) 2000.
Refs: 6.
ISSN: 1335-0013. CODEN: KIALEZ. Pub. Country: Slovakia. Language: Slovak. Summary Language: English; Slovak.
AB Allergen immunotherapy using a standardised modified allergen extracts has been used for successful treatment of type I allergy for many years. All constituents of allergy vaccines are subject of analysis to improve the standardisation of vaccines over last decade. Method of new approaches for this shows this impartion.

L14 ANSWER 7 OF 18 MEDLINE DUPLICATE 5
1999362317 Document Number: 99362317. PubMed ID: 10431101. Comparison of the efficacy and safety of two preseasonal regimens of glutaraldehyde modified, **tyrosine-adsorbed** parietaria pollen extract over a period of three years in monosensitive patients. Negro J M; **Wheeler A W**, Hernandez J; Youlten L J; Pascual A; Garcia-Selles F J; Pagan J A; Lopez-Sanchez J D; Miralles J C; Sarrio F; Milan J M; Contreras L G; Vidal D. (Allergology Section, H. U. "Virgen de la Arrixaca", El Palmar, Murcia, Espana.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1999 May-Jun) 27 (3) 153-64. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.
AB The purpose of this study was to evaluate the clinical efficacy over a period of three years (1988-90) of two preseasonal dosage regimens of a Parietaria allergoid (Bencard **Tyrosine** Parietaria) in patients who were only sensitive to this pollen. Fifty patients were included (14 men and 36 women, age: mean, 28 years; range, 14-47 years). Twenty five patients (group A) were treated each january with the basic course of Bencard **Tyrosine** Parietaria. This consisted of injecting subcutaneously 0.5 ml from each of three vials, with one week between each injection. A further injection using the vial with the highest dose was given one week later. Each january and february, twenty five patients (group B) were treated with the basic course of Bencard **Tyrosine** Parietaria, repeating the last dose five times, with one week between each injection. Immunotherapy with a **tyrosine-adsorbed** Parietaria judaica allergoid is an effective method for mitigating nasal ($p < 0.0001$), bronchial ($p < 0.005$), conjunctival ($p < 0.001$) and palatal itching symptoms ($p < 0.0001$) in patients who are sensitive to this pollen. Sensitivity to Parietaria pollen, as verified by skin test and nasal challenge, decreased during immunotherapy ($p < 0.001$). Histamine release by peripheral blood basophils decreased during the course of the study, falling from 43.5 ng/ml to 12.3 ng/ml in group A and from 42.9

ng/ml to 10.0 ng/ml in group B; during the second and third years, IgG levels were increased one and four months after starting treatment with the extract, while this was not the case after ten months; IgE levels were also increased. Finally, overall tolerance to this immunotherapy product was good in almost all patients.

L14 ANSWER 8 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:155445 Document No.: PREV200000155445. Standardisation of **tyrosine-adsorbed** glutaraldehyde-modified tree pollen extract. **Wheeler, A. W. (1)**; Lees, B. (1). (1) Allergy Therapeutics Ltd., Worthing, BN14 8SA UK. Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 145. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology. ISSN: 0019-2805. Language: English. Summary Language: English.

L14 ANSWER 9 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:155443 Document No.: PREV200000155443. Standardisation of glutaraldehyde-modified allergen **tyrosine-adsorbed** vaccines using an assay system with a Europium label. Newland, B. (1); Lees, B. G. (1); **Wheeler, A. W. (1)**. (1) Allergy Therapeutics Ltd., Worthing, BN14 8SA UK. Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 144. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology. ISSN: 0019-2805. Language: English. Summary Language: English.

L14 ANSWER 10 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:155433 Document No.: PREV200000155433. Standardisation of glutaraldehyde-modified allergen **tyrosine-adsorbed** vaccines containing the TH-1-inducing adjuvant, MPL. Hopkins, M. (1); Lees, B. G. (1); Richardson, D. W. G. (1); **Wheeler, A. W. (1)**. (1) Allergy Therapeutics Ltd., Worthing, BN14 8SA UK. Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 141. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology. ISSN: 0019-2805. Language: English. Summary Language: English.

L14 ANSWER 11 OF 18 MEDLINE DUPLICATE 6
94115598 Document Number: 94115598. PubMed ID: 1669569. Pollinex Parietaria (Bencard Parietaria), a new allergoid for treatment of patients sensitive to Parietaria pollen. Resta O; Carnimeo N; Foschino M P; Taylor I; **Wheeler A W**; Youlten L J. (Cattedra Fisiopatologia Respiratoria Ospedale Policlinico, Bari, Italy.) JOURNAL OF INVESTIGATIONAL ALLERGOLOGY AND CLINICAL IMMUNOLOGY, (1991 Apr) 1 (2) 129-37. Journal code: 9107858. ISSN: 1018-9068. Pub. country: Spain. Language: English.
AB Two matching groups each of eleven patients suffering from allergy to Parietaria pollen were treated either with **tyrosine-adsorbed** glutaraldehyde-modified extract of Parietaria judaica pollen (Bencard Parietaria/Pollinex Parietaria) or with alum-**adsorbed** pyridine-extract (Alavac). The side effects of therapy were similar in both groups and were mostly local in nature. Nasal symptoms were significantly less at the end of treatment in the group of patients treated with Pollinex. P. judaica-specific IgG levels were significantly higher in patients following treatment with Pollinex. The majority of patients in both groups showed reduced nasal and/or skin sensitivity following therapy as measured by provocation testing. The results indicate that Pollinex Parietaria is an effective vaccine for the treatment of immediate hypersensitivity to Parietaria pollen.

L14 ANSWER 12 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1991:313676 Document No.: BA92:24191. STANDARDIZATION OF GLUTARALDEHYDE-MODIFIED **TYROSINE-ADSORBED** ALLERGEN EXTRACTS. OVERELL B G; SPACKMAN D A; **WHEELER A W**; PFEIFER P. STRESEMANNALLEE 6, W-4040 NEUSS 1.. ALLERGOLOGIE, (1991) 14 (3), 110-115. CODEN: ALLRDI. ISSN: 0344-5062. Language: German.

AB A new assessment of the allergoid properties of glutaraldehyde-modified grass pollen extract has been made in order to validate standardization procedures. Increasing substitution of amino groups with glutaraldehyde led to a loss of allergenicity of extracts, as measured by RAST inhibition and by histamine release from sensitized human basophils. Both modified and unmodified materials induced IgG antibody in guinea-pigs. The antibody-stimulating capacity of the modified matrials could not be accounted for by the presence of unmodified activity in the modified samples. The antibodies induced by modified materials had a spectrum of specificities similar to that induced by unmodified extract, these specificities appearing to be directed at allergenic components when assessed by SDS-PAGE immunoblotting. One such specificity was to a major allergen component R7 (Lol p I) of temperate grass pollen. Since immunoreactivity with rabbit IgG antibody specific for R7 was retained in all the modified samples, a basis for an assay for standardization of glutaraldehyde-modified allergen products was established. The rationale for the use of this assay, and its use in establishing "standardized unit" system is explained.

L14 ANSWER 13 OF 18 MEDLINE DUPLICATE 7
94115589 Document Number: 94115589. PubMed ID: 1669563. Hyposensitization therapy of Parietaria-sensitive patients with a **tyrosine adsorbed** allergoid, Pollinex Parietaria (Bencard Parietaria). Bonifazi F; Antonicelli L; Bilo M B; Pucci S; Taylor I H; **Wheeler A W**; Youlten L J. (Servizio Allergologia Respiratoria, Ospedale Generale Umberto I, Ancona, Italy.) JOURNAL OF INVESTIGATIONAL ALLERGOLOGY AND CLINICAL IMMUNOLOGY, (1991 Feb) 1 (1) 37-44. Journal code: 9107858. ISSN: 1018-9068. Pub. country: Spain. Language: English.

AB Thirty patients suffering from allergy to Parietaria pollen were treated with either a new **tyrosine-adsorbed** allergoid of Parietaria judaica pollen (Pollinex Parietaria) or a commercially available alum-**adsorbed** extract (Alavac) as control. A reduced response to nasal provocation was seen in 7 out of 11 patients following treatment with Pollinex and 1 out of 10 after control treatment. 9 out of 11 and 3 out of 10, respectively, showed reduced skin test activity. Patients who received Pollinex tended to have fewer nasal symptoms during the pollen season. Pollinex induced larger increases in P. judaica-specific IgG antibody than did the control product. Side effects of therapy were similar between the two groups of patients. Pollinex Parietaria thus shows good potential for the control of allergy to Parietaria pollen.

L14 ANSWER 14 OF 18 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
90085589 EMBASE Document No.: 1990085589. [Studies on the immunogenicity of tyrosin-**adsorbed**, glutaraldehyde-modified extracts of birch, alder and hazel tree pollens (TA Baumpollen)]. UNTERSUCHUNGEN ZUR IMMUNOGENITAT VON TYROSIN-ADSORBIERTEN, GLUTARALDEHYDE-MODIFIZIERTEN EXTRAKTEN DER BAUMPOLLEN VON BIRKE, ERLE UND HASEL (TA BAUMPOLLEN). Hickman B.E.; **Wheeler A.W.**; Fox B.; Nusslein H.G.; Renner B.. Bencard Allergy Research Unit, Beecham Pharmaceuticals, Yew Tree Bottom Road, Epsom KT18 5XQ, United Kingdom. Allergologie 13/1 (16-20) 1990. ISSN: 0344-5062. CODEN: ALLRDI. Pub. Country: Germany. Language: German. Summary Language: English.

L14 ANSWER 15 OF 18 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 8
87197228 EMBASE Document No.: 1987197228. Oral hyposensitisation with

enteric-coated allergens as extension therapy following a basic subcutaneous course of injections. Horak F.; **Wheeler A.W.**. Bencard Allergy Unit, Beecham Pharmaceuticals, Great Burgh, Epsom, Surrey KT18 5XQ, United Kingdom. International Archives of Allergy and Applied Immunology 84/1 (74-78) 1987.
CODEN: IAAAAM. Pub. Country: Switzerland. Language: English.

AB We investigated in grass-pollen-sensitive adults the efficacy and safety of a therapeutic hyposensitisation regimen consisting of a basic pre-seasonal course of **tyrosine-adsorbed** glutaraldehyde-modified grass pollen extract (Pollinex), followed by oral extension treatment using encapsulated, particulate, enteric-coated grass pollen allergen. The daily recorded symptom scores both of these patients and of others treated with complete basic and extension courses of Pollinex indicated that both sets of patients had fared better during the grass pollen season than control patients who had received only the basic Pollinex injections.

L14 ANSWER 16 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1987:7071 Document No.: BA83:7071. HYPOSENSITIZATION OF PATIENTS WITH POLLINOSIS USING A **TYROSINE-ADSORBED** GLUTARALDEHYDE-MODIFIED TREE POLLEN ALLERGOID CLINICAL AND IMMUNOLOGICAL STUDIES. NUESSLEIN H G; KLEINLEIN M; MANGER B J; KRAPF F E; KAMPMANN B; CLARKE A J; **WHEELER A W**; KALDEN J R. KRANKENHAUSSTR. 12, D-8520 ERLANGEN.. ALLERGOLOGIE, (1986) 9 (9), 381-388. CODEN: ALLRDI. ISSN: 0344-5062. Language: German.

AB Patients [32] with an allergy to tree pollen were treated preseasonally by six injections of a **tyrosine-adsorbed** glutaraldehyde-modified allergoid from birch, alder and hazel pollen (TA-Baumpollen). The efficacy of the hyposensitization was assessed by evaluation of the daily symptom score during the pollen season as compared to the score obtained from the previous year. A marked beneficial effect of the treatment was demonstrated by improvement of conjunctivitis in 78%, rhinitis in 87% and asthma in 65% of the patients. Several immunological parameters were monitored during therapy and during the tree pollen season. Before starting hyposensitization IgE-antibodies specific to birth pollen were detected in all patients, and birth pollen induced histamine release was positive in 31 patients. Both parameters did not change significantly during the observation period, particularly the seasonal rise of specific IgE-antibodies known in untreated patients did not occur. Birch pollen specific IgG antibodies, however, increased significantly during the hyposensitization therapy. Nine patients, who were treated again in a second year, showed a further clinical improvement in 10%; the course of the in vitro parameters did not differ from that recorded in the previous year.

L14 ANSWER 17 OF 18 SCISEARCH COPYRIGHT 2002 ISI (R)
86:539079 The Genuine Article (R) Number: E1308. HYPOSENSITIZATION OF PATIENTS WITH POLLINOSIS USING A **TYROSINE-ADSORBED** GLUTARALDEHYDE-MODIFIED TREE POLLEN ALLERGOID. NUSSLEIN H G (Reprint); KLEINLEIN M; MANGER B J; KRAPF F E; KAMPMANN B; CLARKE A J; **WHEELER A W**; KALDEN J R. UNIV ERLANGEN NURNBERG, INST POLIKLIN KLIN IMMUNOL & RHEUMATOL, D-8520 ERLANGEN, FED REP GER. ALLERGOLOGIE (1986) Vol. 9, No. 9, pp. 381-388. Pub. country: GERMANY. Language: German.

L14 ANSWER 18 OF 18 MEDLINE DUPLICATE 9
82264333 Document Number: 82264333. PubMed ID: 7107028. l-**Tyrosine** as an immunological adjuvant. **Wheeler A W**; Moran D M; Robins B E; Driscoll A. INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1982) 69 (2) 113-9. Journal code: 0404561. ISSN: 0020-5915. Pub. country: Switzerland. Language: English.

AB A series of experiments has been carried out to investigate the adjuvant properties of the amino acid L-**tyrosine** in laboratory animals. Adsorption of various allergenic materials to L-**tyrosine** was

found to enhance the induction of IgG antibodies, but no unusual propensity to stimulate IgE antibody or delayed hypersensitivity was observed. Administration of the amino acid at a site remote from the allergen was found not to augment antibody production. This, together with evidence of reduced bioavailability of the **tyrosine-adsorbed** allergen, suggested that the adjuvant activity observed resulted from a short-term depot effect.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y